II. Remarks

Claims 1, 2, 4, 5, 7-12 and 39-52 are pending.

A. Obviousness-type Double Patenting Rejection

In the instant Office Action, a nonstatutory obviousness-type double patenting rejection has been maintained for claims 1, 2, 4-5, 7-12 and 51-52 as being unpatentable over claims 20, 21 and 23-27, and for claims 39-42 and 46-50 as being unpatentable over claims 25-27 of U.S. Patent No. 6,103,219. An obviousness-type double patenting rejection has also been maintained against claims 39-42 and 46-50 as being unpatentable over claims 19, 20, 24, 30, 32 and 33 of U.S. Patent No. 6,746,693.

These rejections were maintained because the application number cited in the Terminal Disclaimers mailed on April 14, 2008 were incorrect due to a typographical error. New Terminal Disclaimers properly referencing the instant application number and citing both U.S. Patent Nos. 6,103,219 and 6,746,693 are submitted herewith. Applicants believe this submission of the Terminal Disclaimers obviates all outstanding obviousness-type double-patenting rejections, and respectfully request withdrawal of these rejections.

B. 35 U.S.C. §103 Rejections

Removal of the Examiner's obviousness rejection of claims 1, 2, 4, 5, 7-12 and 39-52 under 35 U.S.C. §103(a) as being unpatentable over United States Patent No. 4,605,666 to Schmidt et al. ("Schmidt") is acknowledged with appreciation.

In the Office Action, the Examiner also rejected claims 1, 2, 4, 5, 7-12 and 39-52 under 35 U.S.C. §103(a) as being unpatentable over United States Patent No. 4,910,023 to Botzolakis et al. ("Botzolakis"). The Examiner stated that "*Botzolakis teaches 'various unpleasant flavored*

drugs can be processed by a unique wet granulation process wherein a slurry of the drug in water is dried in combination with colloidal silicon dioxide and, in a particular preferred embodiment microcrystalline cellulose is used with the colloidal silicon dioxide adsorbing on the drug particles' (Col. 2, lines 11-17)" The Examiner also stated "*Botzolakis does not expressly teach drying a slurry of microcrystalline cellulose and silicon dioxide before mixing with a moisture-sensitive active agent.*"

The Examiner then asserted "*One with ordinary skill in the art would change the addition of drug to the dried microcrystalline cellulose and silicon dioxide* ***mixture in order to optimize the taste making and desired release profile of the drug.***" Emphasis added.

In response, the Examiner's rejection is respectfully traversed. Previously presented independent claims 1 and 39 are set forth below:

> Claim 1: A method for preparing a tablet, consisting essentially of the steps of:
>
> forming an aqueous slurry containing a mixture of microcrystalline cellulose in the form of a wet cake and silicon dioxide having a particle size from about 1 nm to about 100 μm;
>
> drying said slurry to obtain an excipient comprising a plurality of agglomerated particles of microcrystalline cellulose in intimate association with said silicon dioxide, the amount of silicon dioxide being from about 0.1% to about 20% relative to the amount of microcrystalline cellulose, by weight;
>
> then mixing a moisture-sensitive active ingredient with said excipient in a ratio from about 1:99 to about 99:1 to obtain a mixture; and compressing said mixture into a tablet.
>
> Claim 39: A method for preparing a tablet, consisting essentially of the steps of:
> (a) forming an aqueous slurry of microcrystalline cellulose in the form of wet cake;
> (b) forming an aqueous slurry of silicon dioxide having a particle size of

from about 1 nm to about 100 μm;
(c) separately introducing said microcrystalline cellulose slurry and said silicon dioxide slurry separately into a drying apparatus for combination therein, to obtain an excipient comprising a plurality of agglomerated particles of microcrystalline cellulose in intimate association with said silicon dioxide, the amount of silicon dioxide being from about 0.1% to about 20% relative to the amount of microcrystalline cellulose, by weight; then
(d) mixing a moisture-sensitive active ingredient with said excipient in a ratio of from about 1:99 to about 99:1 to obtain a mixture; and
(e) compressing said mixture into a tablet.

The claimed invention provides dry agglomerated particles of microcrystalline cellulose in intimate association with silicon dioxide. As set forth at page 22, lines 21-22 of the originally filed application, coprocessing of the microcrystalline cellulose with colloidal silicon dioxide results in monoparticulates wherein the microcrystalline cellulose and the colloidal silicon dioxide are in intimate association, which is synonymous with "integrated" or "united".

1. The Examiner's Proposed Modification of Botzolakis is Incorrect and Unsupportable.

It is respectfully submitted that one of skill in the art would not change the Botzolakis process by adding the drug to the dried microcrystalline cellulose and silicon dioxide mixture of the presently claimed invention in order to optimize taste making as the Examiner has asserted. As described below, this modification would not result in the required protective coating of colloidal silicon dioxide onto the maltasting drug particles to provide taste masking of a maltasting drug.

Botzolakis describes a wet granulation process wherein the drug is prepared into an aqueous slurry with colloidal silicon dioxide (Example 1) or the drug is dissolved in water with colloidal silicon dioxide (Example 2) with colloidal silicon dioxide adsorbing onto the drug particles protective coating which masks the taste of the drug. (Col. 2. lines 12-25.) Botzolakis also alleges that microcrystalline cellulose is added to the mixture as a drying adjunct and a

filler/binder. (Col. 2, lines 48-52.)

In fact, the Examiner has taken the position, without any supportive evidence whatsoever, that one would modify Botzolakis by coating not the drug, but rather the filler or drying adjunct, to optimize taste masking. Since there is no supportive evidence cited by the Examiner that agglomerated microcrystalline cellulose/colloidal silicon dioxide would provide taste masking of a drug, let alone optimize taste masking, the Examiner's rejection cannot stand. In fact, it appears that the Examiner has chosen an unsuitable motivation, and followed that with a hypothetical, unproven and apparently incorrect conclusion.

Botzolakis fails to provide any teaching, suggestion or motivation for modify the alleged process to create dry monoparticulates where microcrystalline cellulose and colloidal silicon dioxide are in intimate association or united. To the contrary, Botzolakis requires that the colloidal silicon dioxide be available to be adsorbed onto the maltasting drug particles creating a protective coating for taste-masking.

Therefore, Botzolakis describes formulations where microcrystalline cellulose is not in intimate association with colloidal silicon dioxide. The Examiner's basis for this modification is faulty and unsupportable. The rejection has been overcome and should be removed. ; and

Moreover, Botzolakis fails to provide a basis for a person having ordinary skill in the art at the time of the invention to form a "pre-manufactured" excipient comprising agglomerated particles of microcrystalline cellulose in intimate association with the silicon dioxide, prior to the addition of a moisture-sensitive active agent, which advantageously protects the moisture-sensitive active, as provided by the subject invention. Instead, Botzolakis teaches adding the drug to water in Example 1 and dissolving the drug in water in Example 2. These processes, required to create the taste masking coatings in Botzolakis, are directly contrary to the goal of

protecting the moisture-sensitive active agent in the present invention.

2. The Examiner's Proposed Modification Would Render the Prior Art Unsatisfactory for its Intended Purpose

If a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. In re Gordon 733 F.2d 900, 221 U.S.P.Q. (Fed. Cir. 1984). See also M.P.E.P. 8th Ed. Rev. No. 6 § 2143.01 (V). In view of the fact that no taste masking properties are attributed to an agglomerated excipient of microcrystalline cellulose/colloidal silicon dioxide, despite a great deal of study by the industry, the Examiner's proposed modification of Botzolakis is untenable because it would render the Botzolakis process unsatisfactory for the stated purpose of providing taste masking of a maltasting drug.

Accordingly, it is respectfully submitted that the Examiner has not established that one of ordinary skill in the art would be motivated to modify Botzolakis to arrive at the invention recited in independent claims 1 and 39. Therefore, withdrawal of the Examiner's rejection of independent claims 1 and claims 2, 4, 5, 7-12, 51 and 52 dependent therefrom; and 39 and 40-50 dependent therefrom is requested.

3. Obviousness Rejections of Claims 2 and 40

Regarding claims 2 and 40, the Examiner asserted "*the limitations of colloidal silicon dioxide and wet granulation prior to compression would have been obvious over the colloidal silicon ... and wet granulation prior to compression, as taught by Botzolakis (Col. 3, lines 39-52).*"

This rejection is respectfully traversed. Claims 2 and 40 further recite wet granulating prior to compressing the mixture of (i) the coprocessed excipient particles of microcrystalline

cellulose in intimate association with colloidal silicon dioxide and (ii) moisture-sensitive active agent, into a tablet. As set forth at page 27, lines 21-25 of the originally filed specification, a representative wet granulation contemplated by the present invention utilizes a granulation liquid mixed with the dry mass to create a powdery mass that has the consistency of damp snow.

By contrast, Botzolakis describes an allegedly unique wet granulation process which requires a slurry of (i) drug, colloidal silicon dioxide and water in Example 1 and (ii) drug dissolved in water with colloidal silicon dioxide in Example 2.

Once again, the Botzolakis process does not form a "pre-manufactured" excipient comprising agglomerated particles of microcrystalline cellulose in intimate association with the silicon dioxide, prior to the addition of a moisture-sensitive active agent, which advantageously protects the moisture-sensitive active, as provided by the subject invention. In other words, the wet granulation step of Botzolakis is used for creating a protective coating of colloidal silicon dioxide over maltasting drug particles for taste-masking drug particles, not for forming granules for tableting. These are two separate and distinct types of wet granulation steps, and cannot simply be morphed as equivalent. They are not. Therefore, for these additional reasons, the processes involving an additional wet granulation steps recited in claims 2 and 40 are not obvious over Botzolakis. Accordingly, withdrawal of the Examiner's rejection of claims 2 and claim 7 dependent therefrom; and claim 40 and claim 45 dependent therefrom is respectfully requested.

The Examiner also rejected claims 4-5, 41-44 and 51-52 under 35 U.S.C. §103(a) as being unpatentable over Botzolakis in view of United States Patent No. 4,605,666 to Schmidt et al. ("Schmidt"). The Examiner stated "*Botzolakis does not expressly teach spray drying. Schmidt teaches a 'process for preparing a powder ... which is directly compressible into a tablet prepared by spray drying (a) an aqueous slurry of a water-soluble vitamin and a binder,*

(b) ... an adsorbent and (c) a lubricant (Abstract)." The Examiner then asserted "*it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of making a tablet ... as taught by Botzolakis, vary the addition of a moisture sensitive active ingredient to the slurry containing colloidal silicon dioxide and microcrystalline cellulose during the process of routine optimization, combine it with the process of spray drying to produce a compressible powder, and produce the instant invention.*"

The Examiner's rejection is respectfully traversed. The Examiner has relied on a combination of Botzolakis and Schmidt in a further modified, unsupportable manner to create a new invention of her own design. It is respectfully submitted that the modifications that the Examiner suggests be done in order to combine these references in any meaningful way is simply a fabrication which is not supportable by any factual basis. The Examiner's proposed (combined) process would ignore required steps by Botzolakis making an agglomerate of drug/colloidal silicon dioxide; then adding a new step (varying the addition of another ingredient) not taught in either reference; then modifying a spray drying step described in Schmidt to produce the invention. The Examiner's recreation does not render the claims in question obvious, but rather is an example of an improper use of hindsight based solely on information provided in Applicants' claims.

Dependent claims 4, 41, 42 and 51 (requiring spray-drying) and dependent claims 5, 43, 44 and 52 (requiring a bulk density of from 0.2 g/ml to about 0.6 g/ml) obvious. The deficiencies set forth above with respect to Botzolakis are reasserted herein. The deficiencies of Botzolakis are not cured by Schmidt. Schmidt alleges a process where a water soluble vitamin is prepared into an aqueous slurry with microcrystalline cellulose that is spray-dried and silicon dioxide and magnesium stearate added to the drying chamber. Both Botzolakis and Schmidt fail to teach or suggest dry agglomerated particles of microcrystalline cellulose in intimate association with silicon dioxide as recited in the instant claims. Additionally, both Botzolakis

and Schmidt fails to provide a basis for a person having ordinary skill in the art at the time of the invention to form a "pre-manufactured" excipient comprising a plurality of agglomerated particles of microcrystalline cellulose in intimate association with the silicon dioxide, prior to the addition of a moisture-sensitive active agent, which advantageously protects the moisture-sensitive active, as provided by the subject invention. Therefore, the teachings of Botzolakis combined with Schmidt fail to provide all of the limitations of claims 4-5, 41-44 and 51-52. Accordingly, withdrawal of the Examiner's rejection is respectfully requested.

III. Conclusion

In view of the arguments presented, it is respectfully submitted that the present application is now in condition for allowance. An early and favorable action on the merits is earnestly solicited. According to currently recommended Patent Office policy, the Examiner is specifically authorized to contact the undersigned in the event that a telephonic interview will advance the prosecution of the application. No fee is believed to be due for the corrected Terminal Disclaimers. A request for a three-month extension of time to reply to the Office Action along with an authorization for the Commissioner to charge the undersigned's Attorney Deposit Account the requisite fee is enclosed.

Respectfully submitted,
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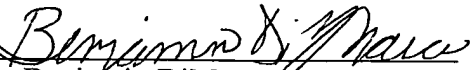
By: 
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